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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/095,536	06/10/1998	JOHN A. KINK	OPHD-03282	9749

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/095,536	KINK, JOHN A.	
	Examiner	Art Unit	
	Joseph F. Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, causa tha application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-18 and 34-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7, 9-18, 34-42, 44-48* is/are rejected.

7)☒ Claim(s) *8 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *03312005*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

In view of the Appeal Brief filed on 1/25/2005, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claims 7-18, 34-48 are pending and under consideration.

The arguments presented in the reply filed 1/25/2005 have been fully considered, but are rendered moot in light of the new rejections set forth below.

The rejection of claims 7-12, 15-18, 34-48 under 35 U.S.C. 103(a) as being unpatentable over U.S. patent No. 5,723,120 (Brakenhoff et al.) in view of Doherty et al. (1992) and further in view of U.S. Patent No. 5,420,253 (Emery et al.) has been withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 9-10, 12, are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,591,827 (Brakenhoff et al.).

The claims are drawn to methods of treatment of sepsis by administration of a preparation comprising antibodies against TNF and IL-6. The language setting forth the components of the composition is open language, such that the composition may also include additional components beyond the enumerated anti-TNF and anti-IL-6 antibodies. The '827 patent discloses methods of administration of an IL-6 receptor antagonist for treatment of sepsis (column 3, lines 14-21). The '827 patent further discloses that agents other than IL-6 receptor antagonists may be included in the composition, and that these other components include antibodies to cytokines (column 12, lines 66-67) specifically, monoclonal antibodies directed to IL-6 and monoclonal antibodies directed to TNF (column 13, lines 1-5). Thus, the '827 patent discloses a method of treatment of sepsis by administration of a composition comprising three components; an IL-6 receptor antagonist, anti-IL-6 antibodies and anti-TNF antibodies. Based upon the open language present in claim 7 setting forth the components of the therapeutic preparation, the method of administration set forth in the '827 patent anticipates the claims. The '827 patent further discloses that the administration can be performed intravenously (column 10, line 44), thus claims 10, 12 are anticipated. The '827 patent discloses that the composition may be administered to treat human patients (column 11, line 67), thus claim 9 is anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7, 9-11, 12-18, 42, 44-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,591,827 (Brakenhoff et al.), in view of U.S. Patent No. 5,585,098 (Coleman et al.).

The claims are drawn to methods of treatment of sepsis by administration of a preparation comprising antibodies against TNF and IL-6. The language setting forth the components of the composition is open language, such that the composition may also include additional components beyond the enumerated anti-TNF and anti-IL-6 antibodies. The '827 patent discloses methods of administration of an IL-6 receptor antagonist for treatment of sepsis (column 3, lines 14-21). The '827 patent further discloses that agents

other than IL-6 receptor antagonists may be included in the composition, and that these other components include antibodies to cytokines (column 12, lines 66-67) specifically, monoclonal antibodies directed to IL-6 and monoclonal antibodies directed to TNF (column 13, lines 1-5). Thus, the '827 patent discloses a method of treatment of sepsis by administration of a composition comprising three components; an IL-6 receptor antagonist, anti-IL-6 antibodies and anti-TNF antibodies. Based upon the open language present in claim 7 setting forth the components of the therapeutic preparation, the method of administration is not patentable over the '827 patent. The '827 patent further discloses that the administration can be performed intravenously (column 10, line 44), thus claims 10, 12 are not patentable. The '827 patent discloses that the composition may be administered to treat human patients (column 11, line 67), thus claims 9, 36 are not patentable. The '827 patent differs from the claimed invention in that it does not disclose methods of administration of antibodies to TNF and IL-6 wherein the antibodies are polyclonal, are avian or chicken antibodies or are derived from chicken eggs, however, U.S. Patent No. 5,585,098 discloses the use of polyclonal antibodies prepared from chicken eggs to neutralize systemic pathogens in mammals (column 4, lines 30-50). Therefore, it would have been obvious to one of skill in the art at the time the invention was made to practice a method of treating patients with sepsis with therapeutic compositions comprising anti-TNF and anti-IL-6 antibodies which are polyclonal, avian or chicken antibodies. The motivation to use antibodies derived from avian sources is provided in the '098 patent which discloses the advantages of egg yolk antibodies (column 5 lines 62-67), including, *inter alia*, that chicken antibodies do not react with mammalian complement, Fc receptors, protein A or protein G. Yolk antibodies show

great acid and heat resistance. Extraction of yolk antibodies can be performed even on a large scale without costly investment. Concentrating the antibody from egg yolk is a relatively straightforward process. Additionally, the '098 patent discloses methods of oral administration of antibodies (column 9, claim1). The antibody is not harmed by pasteurization. The FDA regards egg antibody as a food rather than a drug and has granted GRAS (generally accepted as safe) status thereto (column 5, line 61 to column 6 line 2).

Claims 34-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9108774 (Creasey et al.) in view of Beutler et al. (1985) and further in view of U.S. Patent No. 5,585,098 (Coleman).

The claims are drawn to methods of treatment of sepsis by administration of a preparation consisting of antibodies against TNF and IL-6. The claims are further drawn to methods wherein the inactive ingredient is set forth as albumin, and where the administration is performed intravenously, parenterally, wherein the antibodies are polyclonal, and derived from chicken. The claims are not patentable because the Creasey reference teaches methods of administration of antibody to IL-6 as a prophylactic or treatment of sepsis (page 4, lines 23-24 and page 21, line 19 to page 21, line 13). The anti-IL-6 antibody used in the method of Creasey is a polyclonal antibody (page 8, lines 30-34). The Creasey reference teaches routes of administration include parental and intravenous administration (page 14, lines 12-28). The Creasey reference further teaches that mixtures of antibodies can be used for the treatment of sepsis (page 4, lines 28-31) and additionally details the role of anti-TNF antibodies in the treatment of sepsis (page 1,

line 33 to page 2, line 3). While the Creasey reference does not specifically disclose the administration of a composition consisting of anti-TNF antibodies and anti-IL-6 antibodies to treat sepsis, the Beutler reference teaches methods of administration of antibodies to TNF in a mouse model of sepsis provided protection from the lethal effects of LPS challenge (Figure 3, page 870). These antibodies are polyclonal antibodies (page 1666, column 2, fourth paragraph). This composition administered comprised BSA (page 1666, column 2, third paragraph). Thus, given the teachings of the Creasey reference of the role of anti-TNF antibodies in the treatment of sepsis and the demonstration of the treatment of sepsis with anti-IL-6 antibodies, as well as the teaching of the Beutler reference of the treatment of sepsis with antibodies to TNF, it would have been obvious to one of skill in the art at the time the invention was made to practice a method of treating sepsis by administration of a composition comprising anti-TNF and anti-IL-6 antibodies. The motivation is provided in the Creasey reference which teaches the role of TNF in sepsis as well as the value of the clinical applications of anti-TNF antibodies in the treatment of sepsis (page 2, lines 2-3), and additionally the teaching in the Creasey reference that sepsis can be treated by a mixture of cytokine antibodies (page 4, lines 22-31).

The Beutler and Creasey references differ from the invention set forth in claims 35-41 in that they do not disclose methods of administration of antibodies to TNF and IL-6 wherein the antibodies are avian or chicken antibodies or are derived from chicken eggs, or administered orally, however, U.S. Patent No. 5,585,098 discloses the use of polyclonal antibodies prepared from chicken eggs to neutralize systemic pathogens in mammals (column 4, lines 30-50). Therefore, it would have been obvious to one of skill

in the art at the time the invention was made to practice a method of treating patients with sepsis with therapeutic compositions consisting of anti-TNF and anti-IL-6 antibodies which are polyclonal, avian or chicken antibodies. The motivation to use antibodies derived from avian sources is provided in the '098 patent which discloses the advantages of egg yolk antibodies (column 5 lines 62-67), including, *inter alia*, that chicken antibodies do not react with mammalian complement, Fc receptors, protein A or protein G. Yolk antibodies show great acid and heat resistance. Extraction of yolk antibodies can be performed even on a large scale without costly investment. Concentrating the antibody from egg yolk is a relatively straightforward process. Additionally, the '098 patent discloses methods of oral administration of antibodies (column 9, claim1). The antibody is not harmed by pasteurization. The FDA regards egg antibody as a food rather than a drug and has granted GRAS (generally accepted as safe) status thereto (column 5, line 61 to column 6 line 2).

Conclusion

Claims 8, 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The claims are free of the prior art based upon the arguments set forth in the reply filed 1/25/2005.

Claims 7, 9-18, 34-42, 44-48 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (571) 272-0829.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1646
March 31, 2005

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